APPENDIX A

"CLEAN" VERSION OF EACH PARAGRAPH/SECTION/CLAIM
37 C.F.R. § 1.121(b)(ii) AND (c)(i)

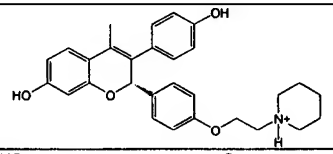
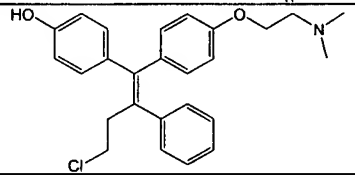
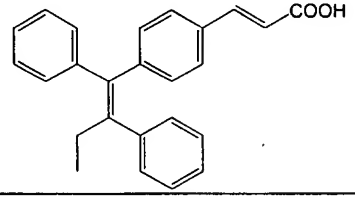
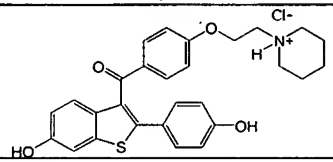
SPECIFICATION:

Replacement for the paragraph beginning at page 25, lines 6-20:

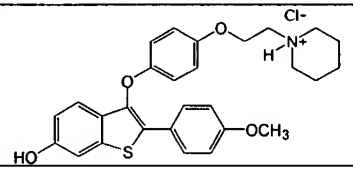
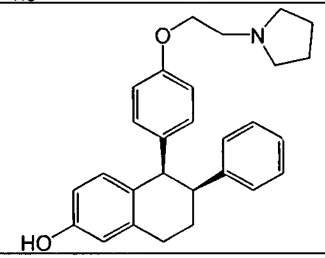
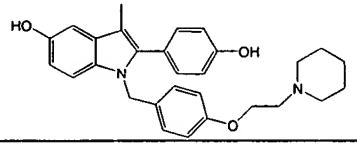
Estrogens are known to lower serum cholesterol but to increase or to have no effect on serum triglycerides levels (Love et al., Ann. Intern. Med. 115: 860-864, 1991; Walsh et al., New Engl. J. Med. 325: 1196-1204, 1991; Barrett-Connor, Am. J. Med. 95 (Suppl. 5A): 40S-43S, 1993; Russell et al., Atherosclerosis 100: 113-122, 1993; Black et al., J. Clin. Invest. 93: 63-69, 1994; Dipippo et al., Endocrinology 136: 1020-1033, 1995; Ke et al., Endocrinology 136: 2435-2441, 1995). Figures 1A and 1B show that EM-800 possesses both hypocholesterolemic and hypotriglyceridemic effects in the rat, thus showing its unique action on the serum lipid profile which is apparently different from other SERMs, such as tamoxifen (Bruning et al., Br. J. Cancer 58: 497-499, 1988; Love et al., J. Natl. Cancer Inst. 82: 1327-1332, 1990; Dipippo et al., Endocrinology 136: 1020-1033, 1995; Ke et al., Endocrinology 136: 2435-2441, 1995), droloxifene (Ke et al., Endocrinology 136: 2435-2441, 1995), and raloxifene (Black et al., J. Clin. Invest. 93: 63-69, 1994). Thus, it is believed that a combination of estrogen and EM-800 should preserved the hypocholesterolemic and hypotriglyceridemic effects of EM-800, thus suggesting that such a combination could exert beneficial effects on serum lipids.

Specification replacement for Table 8 , pages 69 -70:

Table 8

NAME	CODE NAME	STRUCTURE	Maximal stimulation of alkaline phosphatase % of 1nM E_2 stimulation * (nb of experiments)	Inhibition of 1nM E_2-induced stimulation of alkaline phosphatase IC_{50} (nM) (nb of experiments)	Maximal inhibition of 1nM E_2-induced stimulation of alkaline phosphatase (nb of experiments)
EM-652.HCl	EM-652.HCl; (EM-1538)		1.88±0.26 (22)	1.52±0.22 (18)	98.97±0.174 (18)
OH-Toremifene	EM-880		29.6±2.1 (6)	72.1±7.6 (3)	75.73±3.52 (3)
GW-5638	EM-1796		7.75±5.5 (2)	No inhibition	
Raloxifene LY 156758	EM-1105		12.8±1.7 (8)	3.39±0.9 (6)	94.31±1.74 (5)

a2

NAME	CODE NAME	STRUCTURE	Maximal stimulation of alkaline phosphatase	Inhibition of 1nM E_2-induced stimulation of alkaline phosphatase	Maximal inhibition of 1nM E_2-induced stimulation of alkaline phosphatase
LY 353381	EM-1665		15.5±0.25 (5)	1.87±0.07 (2)	90.25±0.127 (2)
Lasofoxifene (free base)	EM-3114		17.9 (1)	4.24 (1)	85.14 (1)
ERA-923	EM-3527		0.6 (1)	5.84 (1)	100.16 (1)

*% of 1nM E_2 stimulation =
OD 405nm compound-OD 405nm basal/ OD 405nm 1nM E_2-OD 405nm basal
Please see also Labrie et al. EM-652 (SCH 57068), a third generation SERM acting as pure antiestrogen in the mammary gland and endometrium, J. Steroid Biochem. and Mol. Bio. 69, 51-84, 1999.